Reviewer's report

Title: Empiric guideline-recommended weight-based vancomycin dosing and nephrotoxicity rates in patients with methicillin-resistant Staphylococcus aureus bacteremia: a retrospective cohort study

Version: 2 Date: 3 October 2012

Reviewer: George Sakoulas

Reviewer's report:

Thank you for the opportunity to review the study by RG Hall et al examining the risk of nephrotoxicity of weight-based vancomycin in patients with MRSA bacteremia. The study is quite straightforward and simple and provides very useful clinical information, serving as yet another example of the uphill battle when employing vancomycin in this situation. I have a few specific comments and concerns. Comments 1-3 must be addressed before acceptance.

1. The authors state that there was no increase in nephrotoxicity when using low dose vs the recommended vanco dosing, yet found obesity as a risk for nephrotoxicity. Given that obese patients receiving low dose could conceivably be receiving higher numbers of grams of vancomycin than high-dose non-obese patients, is the obesity finding simply a reflection of a grams/day risk? Lodise has a study showing risk of nephrotoxicity related to >4g/day so this would be supportive of this. Can the authors clarify?

2. In the beginning of the background section, the authors imply that the vancomycin MIC creep phenomenon preceded the finding of increased failure with vancomycin MIC > 1 mg/L. In fact, the failure with higher MIC’s preceded the creep data, as shown by the dates of publications of references 1-4. The authors should restructure to be more reflective of the temporal relationships of these data.

3. In the patient inclusion data, why were patients with renal dysfunction and those with prior MRSA infection excluded? Only 337 of 798 patients were included for analysis. Authors may want to include this potentially interesting group of patients or explain why they were excluded.

4. Minor comments:
   a. Line 4 of background, would change ‘policymakers’ to “experts in the field’-policymakers sounds like these folks are lawmakers, which they are not
   b. In 3rd line of results section of abstract, would change ‘skin/muscle’ to ‘soft tissue’ as in the text later on

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'